UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,033	11/14/2000	Edward James Rozhon	11133-004-999	9130

20583 7590 01/08/2004

JONES DAY
222 EAST 41ST STREET
NEW YORK, NY 10017

EXAMINER	
MARX, IRENE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 01/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/712,033	ROZHON ET AL.	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40 and 42-75* is/are pending in the application.

4a) Of the above claim(s) *1-20 and 48-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-40,42-47 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The election without traverse filed October 22, 2003 acknowledged. Claims 21-40, 42-47 and 75 are being considered on the merits.

Claims 1-20 and 48-74 are withdrawn from consideration as directed to a non-elected invention.

The status of the parent case(s) should be updated.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-40, 42-47 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague, indefinite and confusing in the recitation "a pharmaceutically effective derivative thereof", because it is unclear which compounds are or are not included therein, even when reading the claims in light of the specification. Which structure components are necessary and/or sufficient to consider a compound a derivative in this context? If applicants intend esters, ethers and oxonium salts, these compounds should be specifically designated as the intended derivatives, provided that there is basis or support therefor in the present written disclosure.

The claims are vague indefinite and confusing in the recitation of "a therapeutically effective amount of ... a pharmaceutically acceptable derivative thereof", since the amount encompassed by this terminology would depend not only on the specific proanthocyanidin polymer or derivative thereof intended but also on the specific disease condition and/or the age and physical condition of the specific individual intended to be treated by administration of the preparation, particularly since the product to be administered is not necessarily purified. Inasmuch as the derivatives are not indicated, it is unclear how an effective amount is to be determined, even if amounts of the compounds per se are mentioned in the current specification. More specifically, there is no indication in the written disclosure of amounts effective to treat conditions as diverse as cholera, ulcerative colitis, irritable bowel syndrome, cancers and neoplasias of the gastrointestinal tract and HIV-associated Chronic Diarrhea. Moreover, the

effective amounts to treat infants or adult humans as well as animals as diverse as poultry, cats, pigs and horses is not delineated with any specificity with respect to "derivatives".

Claim 32 encompasses an improper Markush grouping because of the use of two conjunctive clauses. Proper language is e.g. selected from the group consisting of A, B, AND C. The claims as drafted do not follow this form. See MPEP 2173.05(h)(a).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-40, 42-47 and 75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of traveler's diarrhea with specific doses of proanthocyanidin polymer compositions obtained from *Croton* or *Calophyllum spp.*, does not reasonably provide enablement for the treatment of conditions as diverse as cholera, ulcerative colitis, irritable bowel syndrome, cancers, neoplasias and HIV-Associated chronic diarrhea. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In the instant written disclosure there is no clear and specific indication of a "pharmaceutically effective amount" for each of the diverse compounds to be used and each of the diverse animals to be treated as encompassed by the claimed invention. The specification as-filed does not provide sufficient guidelines or teachings for the treatment of diseases having diverse and even unknown etiologies such as cholera, ulcerative colitis, irritable bowel syndrome, cancers, neoplasias and HIV-Associated chronic diarrhea. It is noted that "cancer" for example encompasses a large variety of disease states and various locations in the gastrointestinal tract may be affect.

In contrast, the specification provides information and data regarding the treatment of one single disease related to secretory diarrhea, i.e., traveler's diarrhea, which is generally caused by bacterial infection. The subjects were administered an initial loading dose of 1250 mg of a specific enteric coated proanthocyanidin polymer composition with three more doses of 250 mg every six hours for the first 24 hours of treatment, and then 500 mg four times per day for a total of 2 grams per day on the second day of dosage. However, there is no indication as to how this

protocol should be adapted to treat the myriad of disease states encompassed by the claimed invention. Moreover, there is no clear indication of the actual components in the compositions used.

The teachings provided in the as-filed specification would not have enabled one skilled in the art to treat secretory diarrhea of any kind including conditions as diverse as cholera, ulcerative colitis, irritable bowel syndrome, cancers, neoplasias and HIV-Associated chronic diarrhea. The guidance provided in the specification is not adequate to lead such persons toward success in treating secretory diarrhea with unspecified proanthocyanidin polymer compositions from *Croton* or *Calophyllum spp.* and pharmaceutical derivatives thereof.

It is apparent that applicant is offering an "invitation to experiment" to those skilled in the art to perform various techniques and to determine for themselves whether they have obtained a suitable proanthocyanidin polymer composition from *Croton* or *Calophyllum spp.* or pharmaceutically acceptable derivative thereof. There is no clear indication of the mode of administration or of the doses required to the treat the multiplicity of disease states encompassed. See Genentech, Inc. v Novo Nordisk A/S., 42 USPQ2d, 1001, 1005 (Fed. Cir. 1997) ("Tossing out the mere germ of an idea does not constitute an enabling disclosure"). Also, In re Scarbrough, 182 USPQ 298, 302 (CCPA 1974) ("It is not enough that a person skilled in the art, by carrying out investigations along the line indicated in the instant application, and by a great amount of work eventually might find out how to make and use the instant invention. The statute requires the application itself to inform, not to direct others to find out for themselves. In re Gardner et al., 166 USPQ 138 (1970)").

Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary to identify the compositions required as well as suitable doses for the treatment of diverse diseases in diverse animals different in requirements; limited amount of guidance and limited number of working examples in the specification directed to the treatment of a specific diarrhea; the unpredictable nature of an invention directed to treating diseases which have diverging causes and effects,, the unpredictability in the art of treatment of disease, and breadth of the claims directed to treatment of any secretory diarrhea. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Thus, the scope of the claims is not commensurate with the teachings of enablement of the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-40, 42-47 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ubillas taken with Masquelier, Wursch and Remington's Pharmaceutical Sciences and applicants' admissions.

Ubillas *et al.* teaches methods of treating diarrhea with pharmaceutical compositions comprising a therapeutically effective amount of proanthocyanidin from *Croton lechleri* in conjunction with milk which is not only a pharmaceutically acceptable carrier, but also is known to protect compositions from the action of stomach acid in the stomach environment because it inhibits stomach acid secretion at least to some extent. The use of proanthocyanidin from *Croton lechleri* is old and well known and been practiced extensively for centuries for various methods of treatment, including the treatment secretory diarrhea, of course. See, e.g., page 78, col. 2, last paragraph.

The reference differs from the claimed invention in the specific formulations and coatings to be provided. However, from the reference it is clear that various formulations are provided in urban health food stores for various therapeutic and prophylactic purposes. In addition, Masquelier recognizes that proanthocyanidin may be administered orally in various stable forms that include coatings, for example (See, e.g., col. 6, lines 43-48) and Wursch teaches that related tannins polymers are administered in various forms that protect compositions from the action of stomach acid, including with milk (See, e.g., Example 12) and coated tablets (See, e.g., example 8).

Moreover, at page 16, first full paragraph of the specification, Applicants disclose that method of making the present formulations is well known in the art, with specific reference being made to "Remington's Pharmaceutical Sciences" (See, e.g., pages 150-533 and pages 1585-1593).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of treatment of diarrhea taught in Ubillas *et al.* by providing compositions of proanthocyanidins for oral ingestion for the treatment of diarrhea which are formulated to protect the proanthocyanidins from the stomach environment, according to the teachings of Masquelier and Wursch for functionally and structurally related polymers and of Remington's Pharmaceutical Sciences for pharmaceutical compositions in general, since the references clearly teach that the technology is well known in the art and for the clear benefits to quality of life of providing compositions for treating secretory diarrhea in the most efficient manner possible.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of sufficient, clear and convincing evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is 703-308-2922. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0926.

Irene Marx
Primary Examiner
Art Unit 1651